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TOXIC EFFECTS OF GASEOUS METABOLIC PRODUCTS ON RATS

[Toksicheskoye deystviye gazoobraznykh produktov zhiznedeyatel'nosti organizma]

by

T. S. Kolosova, L. A. Tiunov, V. V. Kustov, L. V. Ivanova, G. A. Vasil'ev, G. A. Lemesh and M. A. Akhmatova.

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Study of the toxic effect of the complex of gaseous metabolic products involves serious method difficulties. At the present time, more than 400 chemical substances in the composition of so-called "metabolic emissions" have been identified and in a number of cases qualitatively defined; 149 compounds were detected in emissions from the oral cavity, 271 enter the atmosphere from skin impurities, 183 substances are given off from urine and 196 from the feces (Veber, 1967).

To artificially create such a complex of chemical substances for for studying its toxicity for different time periods on the organism

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content of the total organic oxidizable substances by a bichromate method which had the least disadvantages in comparison with permanganate and iodate methods (Ballod, Yegorova, Nefedov et. al., 1967). The content of oxygen and carbon dioxide in the chamber were controlled using an Orsat-Lung instrument.

The test lasted 26 days. Excess carbon dioxide was removed from the chamber using a KhPI absorber; the content of CO_2 in the air of the chamber during the experiment did not exceed 1%. Oxygen was supplied to the chamber automatically. Its concentration was maintained at a level of 19%.

A control group of rats was placed in a vivarium. Study of the atmosphere of the vivarium indicated the presence of the same metabolic products in it as in the inoculation chamber but their content was inconstant and small. For example, of seven air samples taken at different times in the vivarium, in three samples ammonia was not detected at all and in four its content varied from 8 to 16 mg/m^3.

Data on the content of gaseous metabolic products in the inoculation chamber during the test are presented in Table 1.

Periodically (once a week) the animals were weighed. The dynamics of the change in their weight is shown in Figure 1.

As is seen from Figure 1, even in the first week of hermetization, the appearance of a toxic effect in the complex of gaseous metabolic products is apparent, expressed in a slowdown in the growth of the animals.

On the twenty-sixth day of hermetization, the test was stopped. Intensity of consumption of oxygen was studied in 10 of the test and 10

Table 1

The content of gaseous products of metabolism in the inoculation chamber

(2) Вещество	(b) Концентрация, мг/м³ (c) максимальная	(d) минимальная	(3) Вещество	(b) Концентрация, мг/м³ (c) максимальная	(d) минимальная
(1) Окись углерода	50,0	14,0	Ацетон (3)	2,7	0,3
(2) Аммиак	119,2	22,3	Фенол (4)	0,36	0,05

Key: a - Substance
b - Concentration, mg/m^3
c - Maximum
d - Minimum
1 - Carbon monoxide
2 - Ammonia
3 - Acetone
4 - Phenol

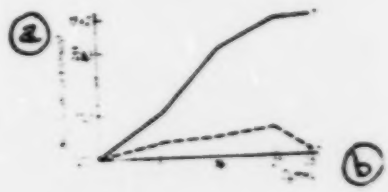

Figure 1. The change in weight of white rats under the effect of gaseous metabolic products. 1 - Control 2 - Test
Key: a - Weight, % of initial
b - Days

of the control animals according to S. V. Miropo'lskiy's method. The results obtained are shown in Table 2.

From the data of Table 2 it is apparent that in the test animals by the twenty-sixth day of the experiment, a statistically proven increase in oxygen consumption is noted.

Table 2

The effect of gaseous metabolic products on the intensity of consumption of oxygen by white rats

(c) номер животного	(a) Опыт: потребление O_2 на 100 г веса (d)	(c) номер животного	(b) Контроль: потребление O_2 на 100 г веса (d)
1	13.28	11	4.48
2	11.00	12	4.58
3	9.46	13	5.75
4	7.03	14	4.83
5	11.55	15	6.37
6	8.96	16	5.09
7	6.75	17	5.45
8	9.02	18	4.47
9	9.10	19	4.80
10	11.4	20	5.59
M	9.82 ± 0.21	M	5.14 ± 0.19
P			<0.001

Key: a - Test
b - Control
c - Number of animals
d - Consumption of O_2 per 100 g of weight

Then, test and control animals were decapitated and subjected to pathomorphological, biochemical and hematological examination.

The numerical material was subjected to statistical processing according to the St'yudent and Fisher method. The data of hematology studies are given in Table 3. From Table 3 it follows that in the test animals one noted a statistically significant decrease in the content of erythrocytes in the peripheral blood. These data agree with the observations of Tomas and Bek (1967) who discovered, with the combined effect of metabolic toxins (indole, skatole, hydrogen sulfide, methyl mercaptan) phenomena of hemolysis and occurrence in the blood of Heinz bodies.

Table 3

The effect of a complex of gaseous metabolic products on the content of regular elements in the blood of white rats

(a) Опыт								(b) Контроль							
(1) Эритроциты	(2) Лейкоциты	(3) Лимфоциты	(4) Сегментоядерные	(5) Палочкоядерные	(6) Эозинофилы	(7) Базофилы	(8) Моноциты	(1) Эритроциты	(2) Лейкоциты	(3) Лимфоциты	(4) Сегментоядерные	(5) Палочкоядерные	(6) Эозинофилы	(7) Базофилы	(8) Моноциты
4,2	3630	62	35	1	1	—	1	5,6	5350	83	15	1	—	—	1
3,8	2400	86	12	1	—	—	1	4,1	4250	83	17	1	—	—	1
3,6	5650	89	26	2	—	1	2	5,4	3500	80	16	2	1	—	1
4,9	2900	71	27	1	—	—	1	5,6	4500	77	20	2	—	—	1
4,1	2400	74	23	2	1	—	—	5,7	4250	76	20	1	1	—	2
2,4	7450	70	27	—	1	1	1	3,5	5050	82	14	2	—	—	2
4,9	6200	73	24	—	1	1	1	5,9	6400	80	18	—	1	—	1
3,8	3500	73	24	1	—	—	2	6,7	5750	79	16	1	1	1	2
5,5	8000	—	—	—	—	—	—	7,2	8750	—	—	—	—	—	—
3,2	7000	—	—	—	—	—	—	6,1	3800	—	—	—	—	—	—
4,04	4617	72,25	24,75	1,0	0,5	0,375	1,125	5,58	5130	81,00	16,75	1,25	0,50	0,13	1,37
M±0,81	±1630	±3,05	±2,8					±0,38	±1380	±0,8	±0,7				

Key: a - Test
b - Control

1 - Erythrocytes
2 - Leucocytes
3 - Lymphocytes
4 - Segment-nuclear
5 - Bacillus-nuclear
6 - Eosinophiles
7 - Basophiles
8 - Monocytes

An analysis of the SH-groups in homogenates of the spleen and in the blood with amperometric titration according to the method of Kolthoff and Harris (1946) was carried out during biochemical study on the experimental and control animals; reduced glutathione in the blood according to Benesch's method (1950) was studied; the activity of catalase in the blood was studied according to the method of A. N. Bakh and R. S. Zubkovaya.

A small increase in the quantity of reduced glutathione in the blood was detected. The content of sulfhydryl groups in the spleen and in the blood in the test animals was practically the same as in the control animals. An increase in catalase activity of the blood was noted in the test rats. The catalase index of the blood was 11 on the average and in the control animals it equaled 0.74.

Determining the index of internal organs in the test animals preceded morphological study. Their sizes are shown in Table 4.

Table 4

Weight indices of internal organs of white rats that underwent inoculation with gaseous metabolic products

a Органы	b Опыт	c Интактные животные (Рылова, 1964)	Органы	Опыт	Интактные животные (Рылова, 1964)
1 Легкие . .	7.91 ± 0.44	2.8—6.75	5 Щитовидная железа . .	0.97 ± 0.09	0.15—0.55
2 Сердце . .	4.94 ± 0.14	2.85—4.4	6 Надпочечники . .	0.35 ± 0.03	0.24—0.36
3 Печень . .	38.37 ± 1.77	28.2—43.5			
4 Почки . .	9.44 ± 0.26	6.3—8.36			

Key: a - Organs
b - Test
c - Intact animals (Rylova, 1964)
1 - Lungs
2 - Heart
3 - Liver
4 - Kidneys
5 - Thyroid gland
6 - Adrenal gland

As is apparent from the data of Table 4, the weight indices of a number of organs in the test rats were increased. An increase in the weight index of the thyroid gland was especially noticeable. Attention was given to the increase in weight indices of lungs and heart.

During pathohistological studies on the lungs of the test rats, the appearance of acute emphysema, an absence of typical alveolar complexes, expansion of alveolar cells, a break in separate membranes

between them with the formation of spur-like protuberances were discovered (Figure 2). In the kidneys – there was a large quantity of albuminous liquid in the openings of the winding channels; there was a sharp plethora of kidney blood vessels down to glomerule capillaries (Figure 3).

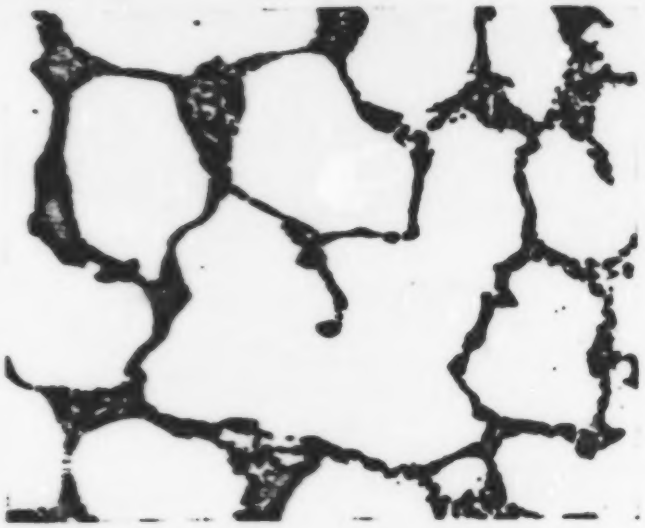

Figure 2. Microphotographs of the lungs. Vesicular emphysema. Elongated alveolae, remains of membranes are visible. Coloration with hematoxylin-eosin. X200

In a specially conducted experiment, the change in some of the indices studied was traced with longer effect of the complex of gaseous metabolic products. Then, it appeared that the decreased content of erythrocytes observed in the 26-day experiment changed to erythrocytosis. The number of erythrocytes in 1 mm^3 of blood reached 7.1± 0.20 million, the catalase index of the blood decreased to 0.59± 0.004; the intensity of consumption of oxygen by the test animals remained high (7.2± 1.2 ml 0_2 per 100 g of weight).

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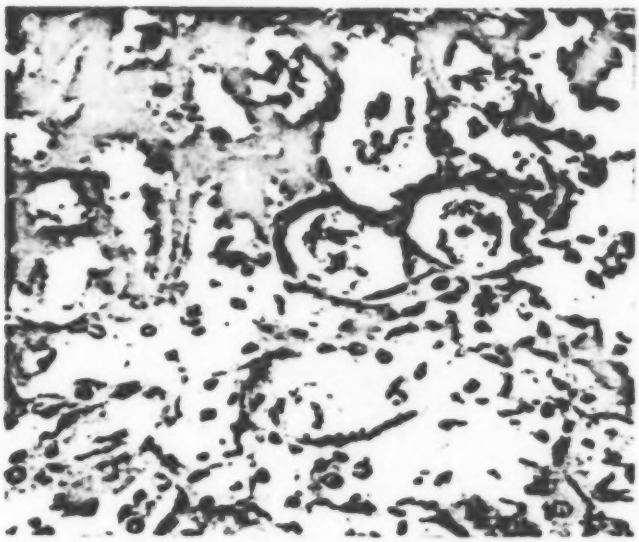

Figure 3. Microphotographs of the kidney. An albuminous liquid in the opening of winding channels. Part of the channels are extended, their epithelia compressed. Coloration with hematoxylin-eosin. X400

A comparison of the results of the experiments done with bibliographical data permits one to note, at first glance, a number of characteristic peculiarities in the biological effect of the entire complex of gaseous metabolic products of the organism. This complex of malodorous, irritating and anoxic toxins with a long term continuous action causes damage to the lung tissue, the development of anemia and results in an increase in oxygen consumption in the test animals. The increase in weight of the thyroid gland gives us information on the phenomena of its hyperfunction. Data on the increase in gas exchange and slowdown in growth of the experimental animals agree with this.

The bibliographical materials also indicate that the experimentally caused increase in the thyroid gland in rabbits is accompanied by a slowdown in

their growth, an increase in frequency of breathing, an increase in the consumption of oxygen (Kakhana, 1968). Among other signs of the toxic effect of gaseous metabolic products one should note the change in activity of catalases of the blood. One can hypothesize that these cyclic changes of catalase activity of the blood have a relationship to the growth of hemolysis. In the composition of the complex of metabolic products there are at least three compounds which suppress activity of the catalases. These are: hydrogen sulfide (Nedolis, 1960), acetone (Dienes, Tofalves, Csotos, 1965), ammonia (Kustov, Mikhaylov, 1966). The decrease in activity of the catalases results in the appearance of effects of endogenic hydrogen peroxide causing a reserve of hemoglobin, the formation of Heinz bodies (Brenner, Allison, 1953) and in the future hemolysis. One should note that the formation of Heinz bodies was observed by A. Tomas and K. Bek (1967) under the effect of a mixture of metabolic toxins. A decrease in the content of erythrocytes results, apparently, in the development of compensating reactions — an increase in the consumption of oxygen, an adaptive increase in the activity of the blood catalases, and in the development of erythrocytosis. A lasting effect causes depletion of the compensatory mechanisms. These data can be added to by bibliographical information on the breakdown of higher nerve activity due to gaseous metabolic emissions (Naumova, 1960), on the effect of some of them on acetylcholine exchange (Kustov et. al., this collection), and on the development of reactions to stress under intoxication of animals with a mixture of certain products of metabolism (Tomas, Bek, 1967).

In conclusion one should note that the study of the biological

effect of the complex of gaseous metabolic products of the organism needs further research.

In this article, only an attempt was made to generalize concerning the particular and bibliographical material existing on this question.

Bibliography

1. Ballod, A. A., L. E. Yegorova, V. A. Koloskoya, Yu. G. Nefedov, L. L. Petrov and V. A. Savina, Problemy sozdaniya zamknytykh ekologicheskikh sistem, [Problems in creating closed ecological systems], Moscow, 133 (1967).

2. Veber, T., Chelovek pod vodoy i v kosmose, [Man under water and in space], Voyenizdat, Moscow, 276 (1967).

3. Yefremova, T. Ye, Opredeleniye vrednykh veshchestv v vozdukhe proizvodstvennykh pomeshcheniy, [Analysis of harmful substances in the air of production rooms], Goskhimizdat Press, Moscow, 345 (1954).

4. Zhitkova, A. S., Ibid., 90 (1954).

5. Kakhana, M. S., Patofiziologiya endokrinnoy sistemy, [Pathophysiology of the endocrine system], "Meditsina" Publ., Moscow, (1968).

6. Kustov, V. V. and V. I. Mikhaylov, Gigiena truda i profzabolevaniya, (3), 6 (1966).

7. Naumova, O. A., "Questions of toxicology and pathophysiology in hygiene," Uch. zap. Moskovskogo NII sanitarii i gigieny im. F. F. Erismana, 3, 60 (1960).

8. Rylova, M. L., Metody issledovaniya khronicheskogo deystviya vrednykh faktorov sredy v experimente, [Methods of studing the chronic effect of harmful factors of the medium in an experiment], "Meditsina" Publ., Moscow, (1964).

9. Salyamon, G. S., Gigiena i sanitariya, 5, 50 (1963).

10. Tomas, A. A. and K. K. Bek, Chelovek pod vodoy i v kosmose, [Man under water and in space], Voyenizdat Press, Moscow, 168 (1967).

11. Filyanskaya, Ye. D., V sb. nauchnykh rabot institutov okhrany truda VTsSPS, [In a collection of scientific works of institutes of labor protection VTsSPS], Profizdat Publ., 4 (1968).

12. Shakhvarger, F. D., citing M. S. Bykhovskaya, S. D. Ginzburg and O. O. D. Khalizova, Prakticheskoye rukovodstvo po promyshlennoy sanitarii khimii, [Practical management of sanitation in the chemical industry], Moscow, 296 (1954).

13. Benesch, K. and K. Benesch, Arch. Biochem., 28 (1), 43 (1950).

14. Brenner, S. and A. Allison, Experimentia, 10, 381 (1953).

15. Dienes, S., K. Tofalvic and A. Csotos, Rev. Med., 11 (2), 146 (1965).

16. Kolthoff, J. and W. Harris, Ind. Eng. Chem. Anal., 18, 161 (1946).